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10/507,502	09/13/2004	Yasuhiro Nishitani	067242-0174	6365

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EXAMINER

BERCH, MARK L

ART UNIT

PAPER NUMBER

1624

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/507,502	Applicant(s) NISHITANI ET AL.	
	Examiner Mark L. Berch	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
 4a) Of the above claim(s) 3 and 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 4-23 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>13 Sept 2004</u> . | 6) <input type="checkbox"/> Other: ____ |

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DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 2, 15-18, 20-21, drawn to Cephalosporins (and oxides), classified in class 540, subclass 222, 225, 227.
- II. Claim 3, drawn to oxacephems, classified in class 540, subclass 301.
- III. Claims 24-26, drawn to starting materials, classified in class 548, subclass 184, 194.

Claims 1, 2-14, 19, and 22-23 are embrative of both Groups I and II, and will be examined to the extent that these read on the elected invention.

The inventions are distinct, each from the other because of the following reasons:

Groups I and II are distinct as seen by their markedly different structures; one contains heterocyclic S but not heterocyclic O, and the other has just the opposite. Cephalosporins and oxacephems are considered distinctly different in the antibacterial art.

Inventions I/II and III are related as mutually exclusive species in an intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product, and the species are patentably distinct (MPEP § 806.05(j)). In the instant case, the intermediate product is deemed to be useful as the preparation of e.g. penicillins and the inventions are deemed patentably distinct because there is nothing on this record to show them to be obvious variants. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because

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the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Alexey Saprigen on 10/24/2006 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-2, 4-23. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3 and 24-26 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1, 2-14, 19, and 22-23 are rejected as being drawn to an improper Markush Group. The claims are drawn to multiple inventions for reasons set forth in the above requirement for restriction. This does not constitute an art recognized genus. Because of the marked structural differences at a part of the molecule essential for utility, the claims are deemed to lack unity of invention (see *In re Harnish*, 206 USPQ 300). The claims are examined only to the extent that they read on the elected invention. Cancellation of the non-elected subject matter will overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-5, 7-8, 10, 15, 20, and 22-23 rejected under 35 U.S.C. 102(b) as being anticipated by Nishimura.

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See Table 2, compounds 10-11. Note that the claim 11 proviso, second branch, excludes 11, but not 10.

Claims 1, 2, 4-5, 7-8, 10, 15, 20, and 22-23 rejected under 35 U.S.C. 102(b) as being anticipated by 4788185.

See examples 92, 108, 109, 110 (top of column 128), 111-112, 133. Note that examples 108, 109-112, 133 all avoid the second branch of the claim 19 proviso.

Claims 1, 2, 4-5, 7-8, 10-11, 15, 20, and 22-23 rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/41128.

See example 14. This is in the ester form, with the amino protected by a formyl group. In claim 11, this correspond to the 5th from last choice, where R3 is hydroxyethyl. Likewise examples 16 and 39 and 48-49(non-protected).

Claims 1, 2, 4-5, 7-8, 10-13, 15-17, and 22-23 rejected under 35 U.S.C. 102(b) as being anticipated by 4427677.

See examples 2, example 3, species (4) and (5), example 5, species 1 and 3, example 6. These are species excluded by the second claim 19 proviso.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 6, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishimura.

The reference is discussed above.

Claims 6 and 9 are drawn to the methylene chain which is substituted by one methyl group. Species 10 and 11, as discussed above, have the methylene chain substituted by zero and two methyl groups respectively. Hence, the chain with one methyl has one more methyl than 10 and one fewer than 11. Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, "The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a *prima facie* case of obviousness of a compound may rest." The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 247; *Ex parte Henkel*, 130 USPQ 474; *In re Jones*, 74 USPQ 152, 154; *In re Herr*, 134 USPQ 176; *Ex parte Dibella*, 157 USPQ 59; *In re Zickendraht*, 138 USPQ 22; *Ex Parte Fischer*, 96 USPQ 345; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39; *In re Bowers and Orr*, 149 USPQ 570. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. As was stated directly in THE

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GENERAL TIRE & RUBBER COMPANY v. JEFFERSON CHEMICAL COMPANY, INC., 182 USPQ 70 (1974): "If any structural change is obvious to one skilled in the art, a substitution of the next higher homolog would seem to be." Note also *In re Jones*, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." See also MPEP 2144.09, second paragraph.

Claims 6, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4788185.

The reasoning is the same as in the previous rejection.

In addition, example 84 renders these claims obvious. This has the methylene with one methyl attached in the A linker. In addition, for claim 6 (but not claim 9), example 85 has methylene with one 3ethyl attached in the A linker. It lacks only the halo on the thiazole. However, the reference teaches that the thiazole with and without the halo are alternatively useable. Note the first structure at column 19, line 53; R2 can be H or Hal as set forth at column 21, lines 12-15. Examples of halothiazoles are seen in 92, 108-112, 133.

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Claims 6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4427677.

The rejection is similar; the reference teaches carboxyalkyl generally in its definition of R2.

Claims 1, 2, 4-5, 7-8, 1013, 15-17, 20, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4550102.

See example 5, species (3). This shows a Chlorothiazole, with an amino-pyridinium, corresponding in claim 12 to the third choice in which R is H. This differs only in the it has, suing the variables of the reference, R2 as methyl rather than R2 as optionally esterified carboxy alkyl. However, the reference teaches the equivalence of such choices in the definition of R2. Further, examples of such R2 as optionally esterified carboxy alkyl choices are seen in example 5, choice (1) and example 3 and example 2, choices (1) and (2).

In addition, note the species example 5, choice (1) and example 3 and example 2, choice (2). These have all aspects of the invention, except for the halogen on the thiazole. However, the reference, in its definition of X, teaches the equivalence of H and Halogen, and example 5, choice (3) proves an example of X=Cl.

Claim 13 has been included, although it is a position isomer, providing for the amino at the 4-position, rather than the 3-position of the reference. However, R3 is depicted as floating, and hence any position would be an obvious variation.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it

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is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The last two lines are unclear. As written, this is part of the Z definition, which makes no sense at all. Applicants presumably mean "or an ester thereof". The next part presumably means "or a compound in which the amino group on the thiazole at the 7-position is protected". Correction is needed if this is what is intended.

1. A protecting group against what? These are final products, so what is there to protect against? As there is no such thing as a universal protecting group, correct selection of a protecting group requires some knowledge of what is being protected against.
2. The definition of Z is garbled. The examiner presumes that this really means "an optionally substituted cationic N atom containing heterocyclic group". As written, the adjective "substituted" has no noun. Slightly different claim language in claim 10 has the same problem.
3. Even assuming that this is the case, it is not clear what this embraces. If there were an N-containing heterocyclic group, and a second non-heterocyclic N, and it was the second N which was the cation, would that be covered?
4. Further, the scope of "group" is unclear. Group is open-ended. For example, the moieties listed in claim 7 all consist of attachment directly to the heterocycle. However, "group"

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would be broad enough to cover e.g. the first choice of claim 11, in which the indicated N is not attached directly to the methylene at the 3-position of cephalosporin, but via a linker of unknown structure. It would cover, in effect, any moiety of any structure, so long as, somewhere, there was a cationic N, and there was a N-containing hetero. It would be unclear what such structures would look like.

5. The word "mono" in the A definition does not make sense.
6. What role does the word "various" have in next to last line of claim 12?
7. Greek letters (or something) have been replaced with boxes in claim 9 and 19.
8. The last term in claim 20 is unclear. Does this mean two lower alkyl groups?

Claims 1-9, 15, 19-20, 22-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

See point 4 above. Because of the unlimited nature of this substituent, it cannot be deemed enabled or even described. For example, the linker is not described, and the present wording would cover a compound with a linker.

Claim Objections

Claims 18, 6, 10 and 11-14 are objected to because of the following informalities: These have a period in the middle of the claim or no period at all. Appropriate correction is required.

Two words run together in the last line of claim 12.

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Claim 15-17 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must be in the alternative only.

The parenthesis need to be removed from the 4th line of claim 18.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663.

The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mark L. Berch
Primary Examiner
Art Unit 1624

3/19/2007